REMARKS

I. Status of the Claims

Claims 1, 4, 8-13, 15, 20-21, 23-29, 35-43, and 48-51 are pending and under examination. Claims 1, 4, 13, 23, and 48-51 have been amended without prejudice or disclaimer. Claims 16-19, 22, and 30-32 were previously withdrawn as being drawn to a nonelected invention. Claims 52-55 have been added. Upon entry of the present amendment, claims 1, 4, 8-13, 15, 20-21, 23-29, 35-43, and 48-55 will be pending and at issue.

II. Amendments to the Claims and New Claims

Claims 1, 4, 13, and 48-51 have been amended without prejudice or disclaimer to recite "consists of" and to delete the term "about." Support for this amendment may be found throughout the specification and in particular on page 3, lines 27-29 to page 4, line 1.

Claim 23 has been amended to recite "a" prior to "therapeutically effective amount" for grammatical clarity.

New claims 52-55 are directed to polypeptides consisting of ATF2 fragments of residues 1-115, 45-75, 45-100, and 50-75. Support for these new claims may be found throughout the specification and in particular on page 3, lines 27-29 to page 4, line 1, and on pages 9-10.

It is believed that the present amendments are in compliance with 37 C.F.R. § 1.116 since no new searching is necessary, and the present amendments are believed to place the claims in condition for allowance. No new matter is added by way of these amendments. Applicants respectfully request reconsideration in view of the remarks and amendments presented herein.

III. Non-Compliant Amendment

Applicants include herewith a corrected version of the "Amendments to the Claims" filed October 31, 2006 (annexed as Appendix 1) with markings in response to

the Notice. In particular, the status identifier for claim 13 has been corrected to recite "currently amended." Claim 13 has also been corrected to show the strikethrough for the term "wild-type." Thus, it is believed that Appendix 1 is fully compliant with 37 C.F.R. §1.121.

IV. Priority Date

The Examiner states that claims 1, 8-12, 35-43, 48, and 50 do not have the benefit of the 35 U.S.C. §119(e) priority date of February 15, 2001 (based on the filing date of Application Serial No. 60/269,118) because these claims are rejected under 35 U.S.C. §112, first paragraph as allegedly lacking adequate written description. The Examiner asserts that in order for a later filed application to receive the benefit of a parent application's filing date, the disclosure of the invention in the parent application and the later-filed application must be sufficient to comply with the first paragraph of 35 U.S.C. §112. Without conceding the validity of the Examiner's assertions, claims 1, 4, 13, and 48-51 have been amended to recite "consists of" and to delete the term "about." Support for this amendment may be found throughout the specification and in particular on page 3, lines 27-29 to page 4, line 1. Thus, it is believed that the amended claims are in compliance with the §112 requirements and that all of the pending claims are entitled to the benefit of the earliest priority date of February 15, 2001.

V. Objection

Claim 23 has been objected to for omitting the article "a" prior to "therapeutically effective amount." In response, claim 23 has been amended to recite "a" prior to "therapeutically effective amount" for grammatical clarity.

VI. Rejections Under 35 U.S.C. §112, Second Paragraph ("Indefiniteness")

The Examiner has maintained the rejection of claims 1, 8-12, and 35-43 under 35 U.S.C. §112, second paragraph, as being indefinite due to the recitation of "Peptide II" in part ii) of claim 1. The Examiner requests clarification of the parenthetical phrase. The Examiner also states that the "Peptide II" fragment described in the specification is not the same as one that includes the phrase "about amino acid residue 50 to about amino

acid residue 100 of ATF2." Without conceding the validity of the Examiner's rejections, claims 1, 4, 13, and 48-51 have been amended to recite "consists of" and to delete the term "about." Applicants point out that the parenthetical reference to "Peptide II" is not intended to be limiting or redefining, but merely is an alternative name for the peptide as it is utilized in the specification. (See page 9, lines 26-27).

Based on the foregoing remarks, Applicants submit that the rejections under 35 U.S.C. § 112, second paragraph, have now been obviated and respectfully request that these rejections be withdrawn.

VII. Rejections Under 35 U.S.C. §112, First Paragraph ("Written Description")

The Examiner has rejected claims 1, 8-12, 35-43, 48, and 50 under 35 U.S.C. §112, first paragraph as failing to comply with the written description requirement. According to the Examiner, the phrases "from about amino acid residue 1 to about amino acid residue 115 of ATF-2" and "from about amino acid residue 45 to about amino acid residue 100 of ATF-2" are new matter lacking support in the application as originally filed.

Without conceding the validity of the Examiner's rejection, claims 1, 4, 13, and 48-51 have been amended to recite "consists of" and to delete the term "about." Support for these amendments may be found, for example, on page 3, lines 27-29 to page 4, line 1 and pages 9-10, where inhibitory N-terminal ATF-2 fragments from amino acids 1-115, 50-100, 45-75, and 45-100 are described.

For at least these reasons, Applicants submit that the rejections under 35 U.S.C. § 112, first paragraph, have now been obviated and respectfully request that these rejections be withdrawn.

VIII. Rejections Under 35 U.S.C. §102

The rejection of claims 13 and 20 under 35 U.S.C. §102 (b) as being anticipated by Livingstone et al., EMBO J. 1995; 14: 1785-97, has been maintained.

Without conceding the validity of the Examiner's rejection, claim 13 has been amended to recite "consists of" and to delete the term "about." Support for this

amendment may be found throughout the specification and in particular on page 3, lines 27-29 to page 4, line 1. Since claim 20 depends from claim 13, it also incorporates this amendment. Because Livingstone discloses an N-terminal ATF2 protein fragment of 112 amino acids it cannot anticipate the claimed polypeptide that consists of the amino acid residues 50 to residue 100 of ATF2. Thus, the rejection in view of Livingstone has been obviated. Accordingly, Applicants request that the Examiner reconsider and withdraw this rejection and allow claims 13 and 20.

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The rejection of claims 1, 8-12, and 35-43 as anticipated by Bhoumik et al. *Clin. Cancer Res.* 2001; 7: 331-42 ("Bhoumik 2001"), as evidenced by Bhoumik et al. (Proc. Natl. Acad. Sci. USA. March 23, 2004; 101(12):4222-4227 ("Bhoumik 2004") has been maintained. The Examiner maintains that since the claims are not supported by the original specification and are not entitled to the earlier priority date, that Bhoumik 2001 anticipates the presently claimed invention.

As described above and without conceding the validity of the Examiner's rejection, claim 1 has been amended to recite "consists of" and to delete the term "about." Claims 8-12 and 35-43 all depend directly or indirectly from claim 1. Support for this amendment may be found throughout the specification and in particular on page 3, lines 27-29 to page 4, line 1. Thus, it is believed that the amended claims are in compliance with the §112 requirements and that all of the pending claims are entitled to the benefit of the earliest priority date of February 15, 2001.

Thus, the rejection in view of Bhoumik 2001 and Bhoumik 2004 has been obviated, since all of the pending claims are entitled to the February 2001 priority date. Accordingly, Applicants request that the Examiner reconsider and withdraw this rejection and allow claims 1, 8-12, and 35-43.

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The rejection of claims 1, 4, 8-10, 12, 13, 20, 23-26, 29, 35-39, 43, and 49-51 under 35 U.S.C. §102(e) as anticipated by U.S. Patent No. 6,579,856 as evidenced by van

Dam et al. (EMBO J. 1995, April. 18; 14(8):1798-1811) and Bhoumik 2004 has been reinstated.

The Examiner has reinstated this rejection relating to the deletion of the term "wild-type." Without conceding the validity of the Examiner's rejection, claims 1, 4, 13, and 48-51 have been amended to recite "consists of" and to delete the term "about." Applicants point out that van Dam does not describe any of the claimed inhibitory peptides and instead only discloses fragments that are 1-112 or 19-96 residues. The only reference to ATF2 in the '856 patent is to the van Dam ATF2 (i.e., fragments that are 1-112 or 19-96 residues). Thus, neither the '856 patent's disclosure, nor van Dam's disclosure of 19-96 or 1-112 fragments of ATF2, anticipate the claimed fragments or methods for inhibiting tumor cell growth utilizing the claimed fragments.

Thus, in view of the present amendments, the rejection in view of U.S. Patent No. 6,579,856 as evidenced by van Dam and Bhoumik has been obviated. Accordingly, Applicants request that the Examiner reconsider and withdraw this rejection and allow claims 1, 4, 8-10, 12, 13, 20, 23-26, 29, 35-39, 43, and 49-51.

IX. Rejections Under §103 (a) Obviousness

The rejection of claims 15 and 21 as being obvious over Livingstone in view of Nilsson et al., *Nucleic Acid Res.* 1985; 13: 1151-62, has been maintained. According to the Examiner, the combined teachings of the references would have made it obvious to make a fusion peptide comprising ATF2 with a translocation peptide, since Livingstone teaches ATF2-Gal4 fusion proteins and Nilsson generally discloses translocation peptides.

As described above and without conceding the validity of the Examiner's rejection, claim 13 has been amended to recite "consists of" and to delete the term "about." Claims 15 and 21 depend directly and indirectly from claim 13. Since Livingstone does not disclose an ATF2 fragment of 50-100 residues (it instead includes additional residues), it cannot be combined with any reference that does not disclose such a fragment to arrive at the presently claimed fragment. Combining Livingstone with Nilsson would result in an ATF2 fragment from residues 1-112 fused to Gal4 or another

translocation peptide. Thus, nothing in Livingstone combined with Nilsson, teaches or suggests the presently claimed fragment.

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Claims 23-29 also stand rejected as obvious over Bhoumik 2001 as evidenced by Bhoumik 2004.

As described above and without conceding the validity of the Examiner's rejection, claim 13 has been amended to recite "consists of" and to delete the term "about." Claims 23-29 all depend directly or indirectly from claim 13. Thus, the rejection in view of Bhoumik 2001 and Bhoumik 2004 has been obviated, since all of the pending claims are entitled to the earliest February 2001 priority date. Accordingly, Applicants request that the Examiner reconsider and withdraw this rejection and allow claims 23-29.

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The rejection of claims 1, 10, 11, 23, 26-28, 35, 39, 40, and 41 under 35 U.S.C. §103(a) as being obvious in view of U.S. Patent No. 6,579,856 as evidenced by van Dam et al. (EMBO J. 1995, April. 18; 14(8):1798-1811) and Bhoumik 2004; in view of Ivanov et al. (Oncogene, 2000; 19:3003-3012) has been reinstated.

A finding of *prima facie* obviousness requires that the combined references teach or suggest all of the claim limitations. As discussed for the anticipation rejection *supra*, the '856 patent, as evidenced by van Dam, does not teach any of the claimed inhibitory N-terminal ATF2 fragments. van Dam does not describe any of the claimed inhibitory peptides and instead only discloses fragments that are 1-112 or 19-96 residues. The only reference to ATF2 in the '856 patent is to the van Dam ATF2 (i.e., fragments that are 1-112 or 19-96 residues). It is noted that neither does van Dam suggest a method of inhibiting or sensitizing tumor cells using any of the claimed ATF fragments. Further, the '856 patent, as evidenced by van Dam, also fails to teach or suggest the claimed fragments since it only refers to van Dam's mutated ATF2 fragment (i.e., the alleged dominant negative).

Finally, Ivanov does not remedy the deficient teachings in the '856 patent or van Dam and does not disclose or suggest the inhibitory ATF2 fragments presently claimed. Therefore, Ivanov cannot be combined with the '856 patent or van Dam to arrive at the presently claimed invention.

Thus, neither the '856 patent, as evidenced by van Dam, nor Ivanov teaches or suggests the inhibitory N-terminal fragments as recited in the claims, and as such, combination of these references also cannot disclose the claimed fragments. For at least the reasons set forth above, pending claims 1, 10, 11, 23, 26-28, 35, 39, 40, and 41 are not obvious over the prior art of record.

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The rejection of claims 13, 15, 21, 23-26, and under 35 U.S.C. §103(a) as being obvious in view of U.S. Patent No. 6,579,856 as evidenced by van Dam et al. (EMBO J. 1995, April. 18; 14(8):1798-1811) and Bhoumik 2004; in view of U.S. Patent No. 6,335,178 has been reinstated. Claims 27 and 28 have been similarly rejected, in view of Ivanov et al.

The Examiner has reinstated this rejection relating to the deletion of the term "wild-type." Without conceding the validity of the Examiner's rejection, claim 13 has been amended to recite "consists of" and to delete the term "about." As described herein, none of the claimed inhibitory peptides encompass the fragments of 1-112 or 19-96 residues as disclosed in van Dam. Furthermore, neither the '856 patent's disclosure of dominant-negative (i.e., mutated) ATF2 with reference to van Dam's 19-96 or 1-112 fragments of ATF2, nor Bhoumik 2004 in view of '178 suggest the claimed methods for inhibiting tumor cell growth utilizing the claimed fragments.

Reconsideration of the claims and withdrawal of the rejections under 35 U.S.C.§ 103(a) is requested.

CONCLUSION

In view of the above amendments and remarks, it is respectfully requested that the application be reconsidered and that all pending claims be allowed and the case passed to issue. Applicants reserve the right to pursue the canceled and/or non-elected subject matter in one or more continuation or divisional applications.

If there are any other issues remaining that the Examiner believes can be resolved through either a Supplemental Response or an Examiner's Amendment, the Examiner is respectfully requested to contact the undersigned at the telephone number indicated below.

Dated: July 23, 2007

Respectfully submitted,

By 

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APPENDIX 1- CORRECTED CLAIM LISTING FROM OCTOBER 31, 2006

IN THE CLAIMS

Please amend the claims as follows:

1. (Currently amended) A method of inhibiting growth of a tumor cell, which method comprises inhibiting transcriptional activity of ATF2 by contacting the cell with an inhibitory N-terminal fragment of ~~wild-type~~ ATF2, wherein the inhibitory N-terminal fragment of ATF2 comprises amino acid residues selected from the group consisting of:

   i. from about amino acid residue 1 to about amino acid residue 115 of ATF-2;

   ii. from about amino acid residue 50 to about amino acid residue 100 (Peptide II) of ATF-2 [[.]];

   iii. from about amino acid residue 45 to about amino acid residue 75 of ATF-2;

   iv. from about amino acid residue 45 to about amino acid residue 100 of ATF-2; and

   v. from about amino acid residue 50 to about amino acid residue 75 of ATF2.

2. (Canceled)

3. (Canceled)

4. (Currently amended) ~~The method of claim 1~~ A method of inhibiting growth of a tumor cell, which method comprises inhibiting transcriptional activity of ATF2 by contacting the cell with an inhibitory N-terminal fragment of ATF2, wherein the inhibitory N-terminal fragment of ATF2 consists essentially of ~~amino acid residues from~~ about amino acid residue 50 of ATF2 to about amino acid residue ~~reside~~ 75 of ATF2.

5. (Canceled)

6. (Canceled)

7. (Canceled)

8. (Original) The method of claim 1 wherein the tumor cell is a melanoma tumor cell.

9. (Original) The method of claim 1, wherein the tumor cell is a breast cancer tumor cell.

10. (Original) The method of claim 1, further comprising treating the tumor cell with a chemotherapeutic agent.

11. (Original) The method of claim 10, wherein the chemotherapeutic agent is selected from the group consisting of a p38 inhibitor, UCN-01, NCS, anisomycin, LY294002, PD98059, AG490, and SB203580.

12. (Previously presented) The method of claim 1, further comprising treating the tumor cell with radiation, wherein the inhibitory N-terminal fragment of ATF2 sensitizes the tumor cell to the radiation.

13. (Currently amended) A polypeptide comprising an inhibitory N-terminal fragment of ~~wild-type~~ ATF2, wherein the inhibitory N-terminal fragment of ATF2 consists essentially of amino acid residues from about residue 50 to about residue 100.

14. (Canceled)

15. (Original) The polypeptide of claim 13, further comprising a translocation peptide sequence.

16. (Withdrawn) A nucleic acid encoding a polypeptide comprising an inhibitory ATF2 N-terminal fragment, which N-terminal fragment comprises a sequence from about amino acid residue 50 to about amino acid residue 75 of ATF2.

17. (Withdrawn) The nucleic acid of claim 16 encoding a polypeptide wherein the N-terminal fragment comprises from about amino acid residue 45 to about amino acid residue 100 of ATF2.

18. (Withdrawn) An expression vector comprising the nucleic acid of claim 16 operably associated with an expression control sequence.

19. (Withdrawn) The expression vector of claim 18, wherein the expression control sequence provides for expression in a tumor cell.

20. (Original) A pharmaceutical composition comprising the polypeptide of claim 13 and a pharmaceutically acceptable carrier or excipient.

21. (Original) A pharmaceutical composition comprising the polypeptide of claim 15 and a pharmaceutically acceptable carrier or excipient.

22. (Withdrawn) A pharmaceutical composition comprising the expression vector of claim 18 and a pharmaceutically acceptable carrier or excipient.

23. (Previously presented) A method of treating a tumor in a subject, which method comprises administering therapeutically effective amount of the pharmaceutical composition of claims 20 or 21, to the subject.

24. (Original) The method of claim 23 wherein the tumor is a melanoma tumor.

25. (Original) The method of claim 23, wherein the tumor is a breast cancer tumor.

26. (Original) The method of claim 23, further comprising treating the tumor with a chemotherapeutic agent.

27. (Original) The method of claim 26, wherein the chemotherapeutic agent is a p38 inhibitor.

28. (Original) The method of claim 26, wherein the chemotherapeutic agent is selected from the group consisting of UCN-01, NCS, anisomycin, LY294002, PD98059, AG490, and SB203580.

29. (Previously presented) The method of claim 23, further comprising treating the tumor with radiation, wherein the inhibitory N-terminal fragment of ATF2 sensitizes the tumor cell to killing by the radiation.

30. (Withdrawn) A method for identifying a compound that modulates ATF2 activity, which method comprises determining the level of expression of a reporter gene in a cell comprising the reporter gene operatively associated with an ATF2-regulated expression control sequence contacted with a compound under conditions in which ATF2 would induce expression of the reporter gene in the absence of the compound, and comparing the level of expression of the reporter gene in the presence of the compound to the level of expression in the absence of the compound, wherein a difference in the level of expression of the reporter gene indicates that the compound modulates ATF2 activity.

31. (Withdrawn) The method of claim 30, wherein the level of reporter gene expression in the presence of the compound is less than in the absence of the compound, wherein the compound inhibits ATF2 activity.

32. (Withdrawn) The method according to claim 31, wherein the compound is a polypeptide.

33. (Canceled)

34. (Canceled)

35. (Previously presented) The method of claim 1, wherein contacting the cell with the inhibitory N-terminal fragment increases the activity of a c-jun family member in the cell, as compared to the activity of the c-jun family member in a tumor cell not contacted by the fragment.

36. (Previously presented) The method of claim 35, wherein the c-jun family member is jun kinase (JNK).

37. (Previously presented) The method of claim 35 wherein the tumor cell is a melanoma tumor cell.

38. (Previously presented) The method of claim 35, wherein the tumor cell is a breast cancer tumor cell.

39. (Previously presented) The method of claim 35, further comprising treating the tumor cell with a chemotherapeutic agent.

40. (Previously presented) The method of claim 39, wherein the chemotherapeutic agent is selected from the group consisting of a p38 inhibitor, UCN-01, NCS, anisomycin, LY294002, PD98059, AG490, and SB203580.

41. (Previously presented) The method of claim 40, wherein the chemotherapeutic agent is a p38 inhibitor.

42. (Previously presented) The method of claim 41, wherein the tumor cell is a late stage melanoma cell.

43. (Previously presented) The method of claim 35, further comprising treating the tumor cell with radiation.

44. (Canceled)

45. (Canceled)

46. (Canceled)

47. (Canceled)

48. (New) A method of inhibiting growth of a tumor cell, which method comprises inhibiting transcriptional activity of ATF2 by contacting the cell with an inhibitory N-terminal fragment of ATF2, wherein the inhibitory N-terminal fragment of ATF2 consists essentially of about amino acid residue 1 of ATF2 to about amino acid residue 115 of ATF2.

49. (New) A method of inhibiting growth of a tumor cell, which method comprises inhibiting transcriptional activity of ATF2 by contacting the cell with an inhibitory N-terminal fragment of ATF2, wherein the inhibitory N-terminal fragment of ATF2 consists essentially of about amino acid residue 50 of ATF2 to about amino acid residue 100 of ATF2.

50. (New) A method of inhibiting growth of a tumor cell, which method comprises inhibiting transcriptional activity of ATF2 by contacting the cell with an inhibitory N-terminal fragment of ATF2, wherein the inhibitory N-terminal fragment of ATF2 consists essentially of about amino acid residue 45 of ATF2 to about amino acid residue 75 of ATF2.

51. (New) A method of inhibiting growth of a tumor cell, which method comprises inhibiting transcriptional activity of ATF2 by contacting the cell with an inhibitory N-terminal fragment of ATF2, wherein the inhibitory N-terminal fragment of ATF2 consists essentially of about amino acid residue 45 of ATF2 to about amino acid residue 100 of ATF2.